

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

Fischetti et al.

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For:

The Honorable Commissioner of
Patents and Trademarks
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#3
Bawa
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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

Applicant provides the following summaries of the enclosed prior art, along with a Form PTO-1449, all of which are enclosed.

U.S. Patent No. 6,264,945 (Fischetti et al.) discloses a method and composition for the treatment of bacterial infections by the parenteral introduction of at least one lytic enzyme produced by a bacteria infected with a bacteriophage specific for that bacteria and an appropriate carrier for delivering the lytic enzyme into a patient. The injection can be done intramuscularly, subcutaneously, or intravenously

U.S. Patent No. 6,254,866 (Fischetti et al) discloses a method which comprises administering a lytic enzyme specific for the infecting bacteria. The lytic enzyme is preferably in a carrier for delivering said lytic enzyme. The bacteria to be treated is selected from the group consisting of *Listeria*, *Salmonella*, *E. coli*, *Campylobacter*, and combinations thereof. The carrier

for delivering at least one lytic enzyme to the digestive tract is selected from the group consisting of suppository enemas, syrups, or enteric coated pills.

U.S. Patent No. 6,248,324 (Fischetti et al.) discloses a method for treatment of bacterial infections of the digestive tract comprising administering a lytic enzyme specific for the infecting bacteria. The lytic enzyme is preferably in a carrier for delivering said lytic enzyme. The bacteria to be treated is selected from the group consisting of *Listeria*, *Salmonella*, *E. coli*, *Campylobacter*, and combinations thereof. The carrier for delivering at least one lytic enzyme to the digestive tract is selected from the group consisting of suppository enemas, syrups, or enteric coated pills.

U.S. Patent No. 6,238,661 (Fischetti et al.) discloses compositions and methods for the prophylactic and therapeutic treatment of bacterial infections which comprise administering to an individual an effective amount of a composition comprising an effective amount of lytic enzyme and a carrier for delivering the lytic enzyme. This method and composition can be used for the treatment of upper respiratory infections, skin infections, wounds, burns, vaginal infections, eye infections, intestinal disorders and dental problems. The claims define the scope of the patent.

U.S. Patent No. 6,056,955 (Fischetti et al.) discloses a method and composition for the topical treatment of streptococcal infections by the use of a lysin enzyme blended with a carrier suitable for topical application to dermal tissues. The method for the treatment of dermatological streptococcal infections comprises administering a composition comprising effective amount of a therapeutic agent, with the therapeutic agent comprising a lysin enzyme produced by group C streptococcal bacteria infected with a C1 bacteriophage. The therapeutic agent can be in a

pharmaceutically acceptable carrier.

U.S. Patent No. 6,056,954 (Fischetti et al.) a method for the prophylactic and therapeutic treatment of bacterial infections i which comprises the treatment of an individual with an effective amount of a lytic enzyme composition specific for the infecting bacteria, with the lytic enzyme comprising an effective amount of lytic enzyme, wherein the lytic enzyme is in an environment having a pH which allows for activity of said lytic enzyme; and a carrier for delivering said lytic enzyme. This method, and composition can be used for the treatment of upper respiratory infections, skin infections, wounds, and burns, vaginal infections, eye infections, intestinal disorders and dental problems. The claims define the scope of this patent.

U.S. Patent No. 6,017,528 (Fischetti et al.) invention relates to compositions containing Group C streptococcal phage associated lysin enzyme for the prophylactic and therapeutic treatment of Streptococcal infections, including the infection commonly known as strep throat. Methods for therapeutically and prophylactically treating such infections also are described.

U.S. Patent No. 5,997,862 (Fischetti et al.) relates to an oral delivery system containing a group c streptococcal phage associated lysin enzyme for the prophylactic and therapeutic treatment of Streptococcal A throat infections, commonly known as strep throat.

U.S. Patent No. 5,985,271 (Fischetti et al) relates to an oral delivery system containing a group c streptococcal phage associated lysin enzyme for the prophylactic and therapeutic treatment of Streptococcal A throat infections, commonly known as strep throat.

U.S. Patent No. 5,688,501 (Merril et al.) is directed to bacteriophage therapy, using methods that enable the bacteriophage to delay inactivation by any and all parts of the host defense system (HDS) against foreign objects that would tend to reduce the numbers of

bacteriophage and/or the efficiency of those phage at killing the host bacteria in an infection. Disclosed is a method of producing bacteriophage modified for anti-HDS purposes, one method being selection by serial passaging, and the other method being genetic engineering of a bacteriophage, so that the modified bacteriophage will remain active in the body for longer periods of time than the wild-type phage.

U.S. Patent No. 4,957,686 (Norris) states that because *S. Sanguis* is the first colonizer of newly cleaned teeth and because other bacteria then attach to it, the formation of dental plaque is reduced on newly cleaned teeth by introducing into the mouth bacteriophages which are parasitic to *S. Sanguis*. Because *S. Sanguis* is the means of attachment of plaque forming bacterial colonies to tooth surfaces and forms 10-15% of the organisms in plaque, destruction of *S. Sanguis* by introduction of its parasitic bacteriophages will remove plaque from teeth surfaces. And removal of plaque containing acid forming bacteria and other harmful bacteria reduces the incidence of dental caries and other disease.

U.S. Patent No. 5,604,109 (Fischetti et al) relates to the rapid detection of Group A streptococci in clinical specimens, through the enzymatic digestion by a semi-purified Group C streptococcal phage associated lysin enzyme and the identification of the released antigens, through the reaction of a labelled ligand and its respective antigen or receptor. The labeled ligand can be included during the digestion of the bacteria, enabling the total assay time to be less than five minutes. The lysin enzyme is stabilized and can be lyophilized for in situ reconstitution. There is no teaching for a specific enzyme to selectively lyse a specific bacteria.

U.S. Patent No. 5,882,631 (Suga et al.) discloses oral compositions containing a water-insoluble noncationic bactericide showing improved stability with time and improved rheologic

properties, and exerting excellent effects of eliminating dental plaque, preventing halitosis and eliminating tooth-staining substances. Addition of porous calcium carbonate to the oral compositions makes it possible to prevent the decrease in the bactericidal activity of water-insoluble noncationic bactericides such as triclosan and improve the stability thereof while exerting excellent effects of eliminating dental plaque, preventing halitosis and eliminating tooth-staining substances. Furthermore, addition of sodium carboxymethyl cellulose to the oral compositions makes it possible to improve rheologic properties and stability with time.

U.S. Patent No.5,741,487 (Asai et al.) discloses an oral composition contains mutanase prepared from a culture which is obtained by cultivating a mutanase-producing microorganism belonging to the genus *Bacillus* having negative protease producibility. The oral composition is effective for suppressing dental plaque formation while the mutanase possesses commercially acceptable stability in the oral composition. The binding of the bacteria is affected by this enzyme; there is no teaching to suggest that the bacteria are being lysed.

U.S. Patent No. 6,113,887 (Mori et al.) disclosed a toothpaste composition containing: (1) a water-soluble bactericide selected from the group consisting of pyridinium compounds, quaternary ammonium compounds and biguanide compounds in an amount of 0.001% to 5.0% by weight, based on the total weight of the composition; (2) a cationically-modified hydroxyethylcellulose having an average molecular weight of 1,000,000 or higher in the hydroxyethylcellulose portion thereof and having a cationization degree of 0.05 to 0.5 mol/glucose in an amount of 0.5% to 5.0% by weight, based on the total weight of the composition; (3) a surfactant selected from the group consisting of polyoxyethylene polyoxypropylene block copolymers and alkylolamide compounds in an amount of 0.5% to 13%

by weight, based on the total weight of the composition; and (4) a polishing agent of the non-silica type in an amount of 5% to 50% by weight, based on the total weight of the composition. An enzyme may be added to the toothpaste, although there is no enzyme added which is specific for a specific bacteria.

U.S. Patent No. 4,122,158 (Schmitt) discloses treating the burned surface of an animal by administering to said surface a contact composition comprising a hydrophobic, bioerodible polymer containing an agent selected from the group consisting of antibacterial, antibiotic, antifungal, proteolytic enzyme and mixtures thereof, which composition when placed in contact with the burned surface maintains homeostasis including prevention of tissue dehydration and thermal loss, and as the polymer bioerodes over time, releases agent to produce a continuous chemoprophylactic or chemotherapeutic effect. Reference is made to the use of enzymes, but none are for specific enzymes which treat a specific bacteria, leaving other bacteria unaffected.

U.S. Patent No. 3,983,209 (Schmitt) discloses a method for treating the burned surface of an animal by administering to said surface a contact composition comprising a hydrophobic, bioerodible polymer containing an agent selected from the group consisting of antibacterial, antibiotic, antifungal, proteolytic enzyme and mixtures thereof, which composition when placed in contact with the burned surface maintains homeostasis including prevention of tissue dehydration and thermal loss, and as the polymer bioerodes over time, releases agent to produce a continuous chemoprophylactic or chemotherapeutic effect. No enzyme is taught which is specific for a specific bacteria.

U.S. Patent No. 6,113,887 (Mori et al) discloses disclosed a toothpaste composition containing: (1) a water-soluble bactericide selected from the group consisting of pyridinium

compounds, quaternary ammonium compounds and biguanide compounds in an amount of 0.001% to 5.0% by weight, based on the total weight of the composition; (2) a cationically-modified hydroxyethylcellulose having an average molecular weight of 1,000,000 or higher in the hydroxyethylcellulose portion thereof and having a cationization degree of 0.05 to 0.5 mol/glucose in an amount of 0.5% to 5.0% by weight, based on the total weight of the composition; (3) a surfactant selected from the group consisting of polyoxyethylene polyoxypropylene block copolymers and alkylolamide compounds in an amount of 0.5% to 13% by weight, based on the total weight of the composition; and (4) a polishing agent of the non-silica type in an amount of 5% to 50% by weight, based on the total weight of the composition. An enzyme may be used in the toothpaste; however, the present invention is not taught, as described previously.

U.S. Patent No. 4,885,163 (Shaar et al.) discloses an invention for promoting the rate and improving the quality of wound healing by topically applying insulin-like growth factor-II to the wound.

U.S. Patent No. 6,132,970 (Stemmer) discloses methods of shuffling polynucleotide variants. The methods entail conducting a multi-cyclic polynucleotide extension process on partially annealed polynucleotide strands having sequences from the plurality of chosen polynucleotide variants, the polynucleotide strands having regions of similarity and regions of heterology with each other and being partially annealed through the regions of similarity, under conditions whereby one strand serves as a template for extension of another strand with which it is partially annealed to generate a population of shuffled polynucleotides. Shuffled polynucleotides are then selected or screened to identify a shuffled polynucleotide having a

desired functional property.

Articles and abstracts which may have pertinence as background art include:

Reisenger, et al. "Characterization of Escherichia coli lysis using a family of chimeric E-L Genes" Fems Microbiol Letter 1998 July 1, 159-167

Seehan MM, et al. "The Lytic Enzyme of the Pneumococcal phage

Young et al. Trends in Microbiology v. 8, n. 4 (March 2000)

Garcia et al. "The Pneumococcal Cell Wall Degrading Enzymes: A modular Design to create New Lysins?" Microb. Drug Resist. 1997 Summer, 3(2): 199-211

Sheehan MM, et al., "The Lytic Enzyme of the Pneumococcal Phage Dp-1: a Chimeric Lysin of Intergeneric Origin" Mol. Microbiol 1997 Aug; 25(4) 717-25

**Garcia P, et al. "Bacteriophages of Streptococcus pneumoniae: a Molecular Approach"
Microb. Drug Resist. 1997 Summer, 3(20) 165-76.**

Sheehan, MM, et al., "Analysis of the Catalytic Domain of the Lysin of the Lactococcal Bacteriophage Tuc2009 by Chimeric Gene Assembling." FEMS Microbiol Lett. 1996 June 15; 14(1): 23-28.

Sanz, JM, et al. "Construction of a Multifunctional Pneumococcal Murein Hydrolase by Module Assembly." Eur. J. Biochem 1996 Feb 1; 235(3):601-5

Lopez R, et al. " Architecture and Domain Interchange of the Pneumococcal Cell Wall Lytic Enzymes" Dev. Biol. Stand 1995; 85:273-81.

Croux, et al. "Interchange of Functional Domains Switches Enzymes Specificity: Contstructin of a chimeric pneumococcal-clostridial cell wall lytic enzyme Mol: Microbiology 1993 Sept; 9(5) 1019-25.

Diaz, E. et al. Chimeric Phage-Bacterial Enzymes: A clue to the Modular Evolution of Genes." PNAS USA 1990 Oct; 87(20) 8125-9.

Diaz, E. et al. "Chimeric pneumoccal Cell Wall Lytic Enzymes Reveal Important. Physiological and Evolutionary Traits." J. Biol. Chem March 25; 266(9) 5464-71.

Lopez, et al. "The Pneumococcal Cell Wall Degrading Enzymes: A Modular Design to Create New Lysins?" Microbiological Drug Resistance, Vol. 3, Number 2, 1997. 199-211.

Loessner, et al. "Evidence for a Holi-Like Protein Gene Fully Embedded out of Frame in the Endolysin Gene of *Staphylococcus aureus* Bacteriophage 187" Journal of Bacteriology, Aug. 1999 p. 4452-4460.

Young, Ry et al. "Phages will out: Strategies of Host Cell Lysis." Trends in Microbiology, Vol. 8, No. 3, March 2000, pp 120-127

Loessner et al. Journal of Bacteriology, August 1999 (p. 4452-4460)

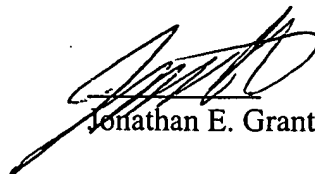
Nelson, et al. "Prevention and Elimination of Upper Respiratory Colonization of Mice by Group A Streptococci by Using a Bacteriophage Lytic Enzyme" PNAS March 27, 2001 vol. 98, no. 7 p. 4107-4112

Garcia, et al. Cloning, "Purification and Biochemical Characterization of the Pneumococcal Bacteriophage Cp-1 Lysin, Journal of Virology, Aug. 1987 p. 2573-2580.

Loessner, et al. "Modified Listeria Bacteriophage Lysin Genes (ply) Allow Efficient Overexpression and One-Step Purification of Biochemically Active Fusion Proteins" Applied and Environmental Microbiology, Aug. 1996 p. 3057-3060

The statement is submitted under the provisions of 37 CFR 1.56 and 1.97(b)(1).

Respectfully submitted,


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